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36. Lancet 2016;pii: S0140-6736(15)01316-1. [Epub ahead of print]
A blood RNA signature for tuberculosis disease risk: a prospective cohort study

Communicable Diseases

1. Am J TMH 2016 Mar 14. pii: 15-0507. [Epub ahead of print]

Differences in Liver Impairment Between Adults and Children with Dengue Infection
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Dengue infection (DI) is a major vector-borne disease in southeast Asia and an important cause of morbidity. The complications such as hepatic impairment are common, and because the physiology of the liver differs between children and adults, the DI-associated liver impairments might be expected to differ as well. This study aims to compare the differences in liver impairment between adults and children with DI. We retrospectively studied 158 adults and 79 children with serologically confirmed DI admitted to the Hospital for Tropical Diseases in Bangkok from 2008 to 2012. In total, 93% of adults and 87% of children exhibited abnormal liver enzyme levels during hospitalization. Overall, 76 (42.4%) adults and 16 (20.3%) children had dengue hemorrhagic fever (DHF). Compared with children, adults with dengue fever (DF) presented a significantly higher incidence of liver function impairment (alanine transaminase [ALT] > 2 × upper limit of normal [ULN]) (47.1% versus 25.5%), hepatitis (ALT > 4 × ULN) (29.4% versus 12.8%), and severe hepatitis (aspartate transaminase [AST]/AST > 10 × ULN) (16.5% versus 4.3%). Children with DHF showed a significantly higher incidence of liver function impairment due to AST derangement than did adults (100% versus 73%). There were no differences in the total bilirubin, albumin, or total protein levels between adults and children. Liver enzymes normalized significantly more slowly in adults, and AST recovery was faster than ALT. In conclusion, liver function impairment was more common among adults than children with DF. As the severity progressed to DHF, liver injury became more common in children.

2. Am J TMH 2016 Mar 28. pii: 15-0867. [Epub ahead of print]

Assessing Perceived Challenges to Laboratory Testing at a Malawian Referral Hospital
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Adequate laboratory infrastructure in sub-Saharan Africa is vital for tackling the burden of infectious diseases such as human immunodeficiency virus and acquired immune deficiency syndrome, malaria, and tuberculosis. Despite the need for laboratory testing in addressing the infectious disease burden, laboratories are ill-integrated into the diagnostic and care delivery process in low-resource settings. There is a diagnostic culture of circumventing laboratory testing and using other, less reliable and less valid signals to diagnose diseases such as malaria. Although much of the literature focuses on disease-specific challenges around laboratory testing, we sought to identify horizontal challenges to the laboratory testing process through interviews with clinicians involved in the diagnostic process. Based on 22 interviews with physicians, nurses, clinical officers, medical students, and laboratory technicians, technologists and supervisors, we identified 12 distinct challenges in the areas of staff, materials, workflow, and the blood bank. These challenges underscore the informational challenges that compound more visible resource shortages in the laboratory testing process, which lend themselves to horizontal strengthening efforts around the diagnostic process.

3. BMJ 2016;352:i178 Editorials

Ebola survivors: not out of the woods yet
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CMO's advice on managing the risk of viral persistence and relapse

The recent outbreak of Ebola virus disease in west Africa was unprecedented in scale, with over 28 600 cases and 11 300 deaths. Survivors may have a range of continuing health problems, including viral persistence and disease recrudescence. If they present with illness, or for certain interventional procedures, they could put others at risk of infection. Clinicians therefore need to know what action to take, and here we lay out the current evidence and expert advice for England.
Studies of survivors from previous smaller outbreaks, corroborated recently, suggest that post-infection sequelae are not uncommon. Fatigue, arthralgia, and ocular complications (including uveitis) are particular problems. The pathogenesis of post-disease complications, and in particular the presence and role of viral persistence, is unknown.
It now seems that earlier prevalence studies underestimated the duration of viral persistence in several immune privileged body sites, such as the testes, eye, and central nervous system. A recent small observational study showed persisting Ebola virus genome in the semen of 26% of male survivors up to nine months after disease onset, much longer than the 91 days previously recognised.

4. BMJ 2016;352:i1049, Clinical Review

Zika virus
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Zika virus is spreading rapidly in the Americas. The virus was identified in the late 1940s in Africa but was first confirmed in Brazil in May 2015. It has since been identified in more than 27 countries and territories in the region. Spread to the Americas was predicted because of the abundance of the mosquito vector, Aedes aegypti. Clinicians worldwide need to be aware of Zika virus infection owing to international travel and the presence of another potentially competent mosquito vector (Aedes albopictus) in North America and southern Europe. Some Brazilian regions experiencing outbreaks of Zika infection have reported an apparent increase in congenital microcephaly and post-infective neurological syndromes, particularly Guillain-Barré syndrome (see boxes 1 and 2). The association of these conditions with Zika virus infection is currently unproved and is under investigation. On 1 February 2016, the World Health Organization declared the recent cluster of microcephaly and other neurological disorders reported in Brazil, following a similar cluster in French Polynesia in 2014, a public health emergency of international concern. If Zika virus infection is confirmed to cause congenital microcephaly, this could lead to a large international burden of infant neurological morbidity. Zika virus infection should be considered in people presenting with compatible symptoms who have recently returned from countries where outbreaks of the infection are occurring. This review provides up to date information at the time of publication on Zika virus, its evolving epidemiology, how to recognise its clinical presentation, possible complications, and how to confirm the diagnosis.
What you need to know
Zika virus, transmitted by mosquitoes, has spread rapidly recently in the Americas, and it is likely to spread further in the presence of Aedes mosquitoes
Zika virus infection causes either a mild illness with fever, rash, conjunctivitis, arthralgia, and myalgia, or it may be subclinical
Some Brazilian regions experiencing outbreaks of Zika virus infection have reported an apparent increase in congenital microcephaly. Some countries experiencing outbreaks have reported an increase in post-infective neurological syndromes, particularly Guillain-Barré syndrome. An association with Zika virus has yet to be confirmed
The situation is changing rapidly, and up to date advice must be sought about travel to affected areas, particularly with regard to pregnancy and sexual transmission

5. BMJ 2016;352:i1062, Practice Pointer

Zika virus: management of infection and risk
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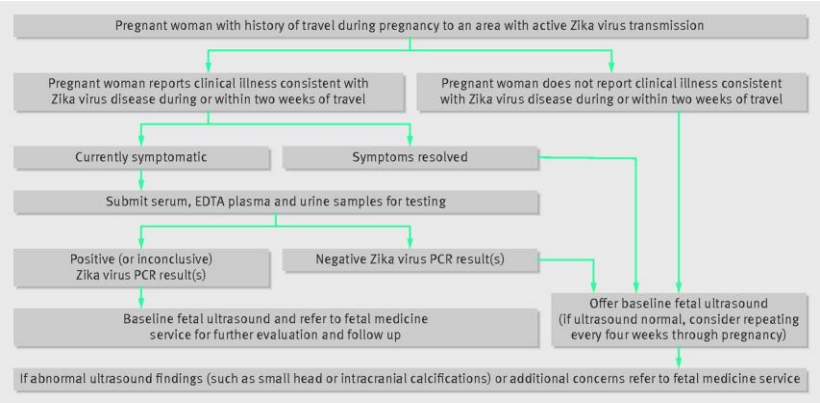
Zika virus produces a mild illness with non-specific symptoms and may be symptomatic in just one in four cases
The link between infection in pregnancy and microcephaly is not fully characterised
Offer pregnant women at risk of infection a monthly fetal scan, and discuss those with symptoms with an infectious disease specialist
Women who are pregnant or planning pregnancy should consider avoiding travel to affected areas
Advise men returning from affected areas to avoid unprotected sex with female partners of childbearing potential for 28 days, and for six months if they have probable or confirmed infection
Testing and monitoring of pregnant women is guided by symptoms
There is an absence of good evidence to guide testing and monitoring. However, expert guidance has been issued by international bodies.



6. HPP 31(2)2016;250–258

A retrospective audit of antibiotic prescriptions in primary health-care facilities in Eastern Region, Ghana

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Resistance to antibiotics is increasing globally and is a threat to public health. Research has demonstrated a correlation between antibiotic use and resistance development. Developing countries are the most affected by resistance because of high infectious disease burden, limited access to quality assured antibiotics and more optimal drugs and poor antibiotic use practices. The appropriate use of antibiotics to slow the pace of resistance development is crucial. The study retrospectively assessed antibiotic prescription practices in four public and private primary health-care facilities in Eastern Region, Ghana using the WHO/International Network for the Rational Use of Drugs rational drug use indicators. Using a systematic sampling procedure, 400 prescriptions were selected per facility for the period April 2010 to March 2011. Rational drug use indicators were assessed in the descriptive analysis and logistic regression was used to explore for predictors of antibiotic prescription. Average number of medicines prescribed per encounter was 4.01, and 59.9% of prescriptions had antibiotics whilst 24.2% had injections. In total, 79.2% and 88.1% of prescribed medicines were generics and from the national essential medicine list, respectively. In the multivariate analysis, health facility type (odds ratio [OR] = 2.05; 95% confidence interval [CI]: 1.42, 2.95), patient age (OR = 0.97; 95% CI: 0.97, 0.98), number of medicines on a prescription (OR = 1.85; 95% CI: 1.63, 2.10) and ‘no malaria drug’ on prescription (OR = 5.05; 95% CI: 2.08, 12.25) were associated with an antibiotic prescription. A diagnosis of upper respiratory tract infection was positively associated with antibiotic use. The level of antibiotic use varied depending on the health facility type and was generally high compared with the national average estimated in 2008. Interventions that reduce diagnostic uncertainty in illness management should be considered. The National Health Insurance Scheme, as the main

purchaser of health services in Ghana, offers an opportunity that should be exploited to introduce policies in support of rational drug use.

7. NEJM 2016;374:501-503

Perspective: A World Free of Polio — The Final Steps
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Global polio-eradication efforts have led to a dramatic decrease in polio cases, from an estimated 350,000 cases in 125 countries in 1988 to 72 cases in 2015. As of January 2016, endemic transmission of polio caused by wild polioviruses (WPVs) had been interrupted in all countries except Pakistan and Afghanistan. Indeed, the Global Commission for Certification of the Eradication of Poliomyelitis recently certified that type 2 wild poliovirus, one of three strains responsible for centuries of human paralysis and disfigurement, has been eradicated. Type 2 poliovirus now exists only in laboratories and in trivalent oral polio vaccine (tOPV) in an attenuated form, though in rare circumstances it surfaces in the community, through persistent transmission, in the form of outbreaks of vaccine-derived viruses. Getting to this point has not been easy. Sustaining our wins and traversing the last mile of the eradication journey calls for escalation of global immunization activities on an unprecedented scale.
Oral polio vaccine (OPV) has been the lynchpin of successful control of paralytic polio. However, in very rare instances, it has been associated with cases of paralysis caused by vaccine-associated paralytic polio (VAPP) or circulating vaccine-derived polioviruses (cVDPVs) — the latter when the viruses included in the vaccine have mutated over time, acquiring the neurovirulence and transmissibility of WPV. For this reason, it is of paramount importance to discontinue the use of OPV after polio eradication has been certified. Since the last case of naturally occurring type 2 WPV in 1999, continued use of OPV2 (the type 2 component of tOPV) has paralyzed an estimated 1600 to 3200 people with VAPP and more than 600 people with type 2 cVDPV. Because routine use of type 2–containing vaccine is no longer needed, the global community has a moral imperative to discontinue it as soon as programmatically feasible. Because WPV types 1 and 3 have not yet been eradicated, however, the phased withdrawal of OPV antigens will begin with a shift from tOPV (containing types 1, 2, and 3) to bivalent OPV (bOPV, containing types 1 and 3).
Global cessation of OPV2 use poses a low but real risk of outbreaks of cVDPV2 or WPV infections associated with declining immunity to type 2 poliovirus. The overarching strategy for reducing this risk is to maximize immunity against type 2 before and after withdrawal of the vaccine and to prepare for an appropriate outbreak response. Doing so requires a comprehensive, multipronged approach (see table Risks and Risk-Mitigation Strategies for Switching from Trivalent Oral Polio Vaccine (tOPV) to Bivalent OPV (bOPV).).
Coordinated communication among global health organizations, countries, manufacturers, and funders is imperative to ensure synchronized OPV2 withdrawal with minimal disruption in vaccination services to children worldwide.
But collaboration in eradication efforts has reached a high point never before achieved by the immunization community. Getting here has required tireless effort and practical innovation in science, policy, and implementation. Capitalizing on the gains made to date should push overall polio eradication over the finish line and may pave the way for measles eradication and future global health initiatives.

8. TMIH 2016;21(3):334-9. Epub 2015 Dec 29

Early- and late-stage ocular complications of herpes zoster ophthalmicus in rural South Africa
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Objectives: To describe the spectrum of ocular complications of herpes zoster ophthalmicus (HZO) in rural South Africa.
Methods: Patients presenting with visual complaints and active or healed HZO at the ophthalmology outpatient department of three hospitals in rural South Africa were included in this study. Demographic and clinical data were collected, and HIV status was determined for all participants.
Results: Forty-eight patients were included, and 81% were HIV infected. Poor vision was reported by 94% of patients, painful eye by 79% and photophobia by 63%. A diverse spectrum of ocular complications was observed with corneal inflammation and opacification in 77% followed by anterior uveitis in 65%. The majority (65%) presented with late-stage ocular complications associated with irreversible loss of vision whereas early-stage complications, such as punctate epithelial keratitis and anterior uveitis, were less common. Blindness of the affected eye was observed in 68% of patients with late-stage complications. There was a considerable delay between onset of symptoms and first presentation to the ophthalmology outpatient department (median time 35 days; range 1-2500 days), and longer delay was associated with late-stage ocular complications (P = 0.02).
Conclusions: HZO patients present with relatively late-stage ocular complications, and blindness among these patients is common. The delayed presentation to the ophthalmology outpatient department of hospitals in our rural setting is of concern, and efforts to improve ocular outcomes of HZO are urgently needed.

Health systems

9. BMJ 2016;352:i244, Editorials

Role of priority setting in implementing universal health coverage
Yot Teerawattananon, et al., Prince Mahidol Award Conference secretariat <alia.l@hitap.net>

Explicit, evidence based priorities are essential for efficient use of resources
When is a country financially ready to implement universal health coverage (UHC), a health policy designed to ensure that all citizens receive the health services they need without financial hardship? Since no standard set of essential health services or a defined benefits package for universal coverage exists, determining financial readiness is challenging. Health priorities must be set knowing what services are to be provided, to whom they will be provided, and how.
Priority setting helps determine the financial requirements for UHC, and thus the financial capacity of a country to adopt it. Setting priorities also helps decide on the benefits package that is feasible given current resource constraints. Countries can deliver a limited benefits package and identify priorities for expansion should additional resources become available. In either scenario, priority setting is essential for any country committed to universal coverage.
Priority setting can be explicit or implicit. Governments should favour explicit rationing, wherein the decisions and their justifications are clear, rather than strategies of implicit rationing such as denial, deterrence, deflection, delay, and dilution. In 2015, the UN General Assembly made a global commitment to UHC and the sustainable development goals. As such, more emerging economies will commit to UHC. Explicit priority setting, however, requires dedicated resources, which are more readily available in wealthier countries.
In 1912, Norway was the first country to introduce UHC. Several other high income countries followed, but 64 years passed before Cuba became the first middle income country to introduce UHC legislation in 1976. By 2015, 58 countries had achieved universal coverage, of which 22 did so while they were low or middle income countries (LMICs). Thus, the challenge that remains is supporting countries with limited capacity to implement UHC and set priorities explicitly.
Health priority setting in support of UHC requires capacity and resources, as well as persuasive evidence to justify decisions. This involves two major steps: evidence generation and use of evidence in resource allocation, programme management, and quality assurance. Priority setting in health

systems is complicated by a wide range of political, economic, ethical, and sociocultural factors. An explicit process requires four building blocks.

Four building blocks for effective priority setting

- Governing structure with clear functions and regulation of institutes and their inter-relations
- Resource availability and mobilisation to support priority setting
- Capacity building programmes for better understanding of health priority setting by policy makers, researchers, and other stakeholders, including the general public
- Collaboration with networks of local, international, and global organisations that aim to support UHC policies.

10. HPP 2016;31:i1–i2

Editorial. Networks and global health governance: Introductory editorial for Health Policy and Planning supplement on the Emergence and Effectiveness of Global Health Networks
Shiffman J

Global health networks are cross-national webs of individuals and organizations linked by a shared concern to address a particular health problem that affects or potentially affects a sizeable proportion of the world's population. Formal institutions anchor some (e.g. the Global Polio Eradication Initiative). Informal ties characterize others (e.g. surgical conditions). For several reasons, these networks deserve greater research attention than they have received.
First, over the past quarter century they have proliferated and now exist for most problems that stand behind high mortality and morbidity in low- and middle-income countries. Secondly, differences in their effectiveness may be one reason some conditions receive greater attention and resources than others. Thirdly, their proliferation represents a shift in the way global health is governed: from a system dominated by hierarchical forms of organization— especially nation-states and intergovernmental organizations— to one also characterized by horizontal networking and growing participation of non-state actors. Fourth is concern about their legitimacy: by what authority, if any, do they exert power?

This supplement presents findings from a research project examining the emergence and effectiveness of global health networks addressing tobacco use, alcohol harm, maternal mortality, neonatal mortality, tuberculosis and pneumonia. The project, funded by a grant from the Bill and Melinda Gates Foundation, brought together 12 investigators from North American, South American and European institutions to investigate three questions:
1. How do global health networks emerge and evolve?
2. What role, if any, do they play in securing attention, raising resources and influencing policy for the conditions that concern them?
3. What factors shape their ability to do so?
The project has a comparative case study design. The six networks are grouped into three matched pairs: two communicable diseases that affect the respiratory system (tuberculosis and pneumonia); two groups vulnerable at birth (pregnant women and newborns); and two addictive substances (tobacco and alcohol). Within each pair, despite comparable or lower disease burden, the first issue has received greater policy attention than the second. We seek to understand why?

Titles in this Supplement:

- A framework on the emergence and effectiveness of global health networks
- The challenge of sustaining effectiveness over time: the case of the global network to stop tuberculosis

- Pneumonia's second wind? A case study of the global health network for childhood pneumonia
- Agenda setting for maternal survival: the power of global health networks and norms
- Network advocacy and the emergence of global attention to newborn survival
- From global agenda-setting to domestic implementation: successes and challenges of the global health network on tobacco control
- The global health network on alcohol control: successes and limits of evidence-based advocacy
- Comparing global alcohol and tobacco control efforts: network formation and evolution in international health governance

11. TMIH 2016;21(4):515-24

Measuring the impact of non-monetary incentives on facility delivery in rural Zambia: a clustered randomised controlled trial
Wang P et al., IDinsight, Lusaka, Zambia

Objectives: In Zambia, only 56% of rural women deliver in a health facility, and improving facility delivery rates is a priority of the Zambian government. 'Mama kit' incentives - small packages of childcare items provided to mothers conditional on delivering their baby in a facility - may encourage facility delivery. This study measured the impact and cost-effectiveness of a US$4 mama kit on rural facility delivery rates in Zambia.
Methods: A clustered randomised controlled trial was used to measure the impact of mama kits on facility delivery rates in thirty rural health facilities in Serenje and Chadiza districts. Facility-level antenatal care and delivery registers were used to measure the percentage of women attending antenatal care who delivered at a study facility during the intervention period. Results from the trial were then used to model the cost-effectiveness of mama kits at-scale in terms of cost per death averted.
Results: The mama kits intervention resulted in a statistically significant increase in facility delivery rates. The multivariate logistic regression found that the mama kits intervention increased the odds of delivering at a facility by 63% (P-value < 0.01, 95% CI: 29%, 106%), or an increase of 9.9 percentage points, yielding a cost-effectiveness of US$5183 per death averted.
Conclusions: This evaluation confirms that low-cost mama kits can be a cost-effective intervention to increase facility delivery rates in rural Zambia. Mama kits alone are unlikely to completely solve safe delivery challenges but should be embedded in larger maternal and child health programmes.

HIV

12. NEJM 2016;374:761-770 Review Article

Campion EW, Editor
Challenges in the Elimination of Pediatric HIV-1 Infection
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Pediatric acquired immunodeficiency syndrome (AIDS) was first described in 1982, 18 months after the first cases were reported in adults. The majority of pediatric infections are acquired through mother-to-child transmission of human immunodeficiency virus type 1 (HIV-1), which can occur during pregnancy, delivery, or breast-feeding. The maternal viral load is a strong independent predictor of the risk of transmission, regardless of timing; transmission rates are extremely low when viral replication is fully suppressed. Before the development of effective preventive interventions, the rate of transmission from mother to child ranged from 15 to 25% among infants who were formula-fed and from 25 to 40% among infants who were breast-fed. One of the greatest public health success stories has been the development and implementation of interventions to prevent mother-to-child transmission of HIV-1. In 1994, the Pediatric AIDS Clinical Trials Group Protocol 076, known as the 076 trial, showed that the single antiretroviral drug zidovudine, given orally to the mother during pregnancy, intravenously during labor, and orally to the newborn for 6 weeks, reduced in utero and intrapartum HIV-1 transmission in infants who were not breast-fed by nearly 70%. This regimen was rapidly adopted in the United States, with a subsequent precipitous decline in the rates of mother-to-child transmission. Observational studies suggested that two- or three-drug antiretroviral regimens given during pregnancy further reduced transmission, as compared with zidovudine alone. Women with HIV-1 infection in resource-rich countries are advised not to breast-feed, since HIV-1 can be transmitted through breast-feeding and since affordable replacement feeding and clean water are available. With the routine use of combination antiretroviral therapy during pregnancy and avoidance of breast-feeding, current mother-to-child transmission rates in the United States and other resource-rich settings are below 1%. However, most pediatric HIV-1 infections occur in resource-limited countries, with the majority (>90%) in sub-Saharan Africa. After the results of the 076 trial were released, international trials initially evaluated short-course regimens of single antiretroviral drugs, with a focus on preventing in utero and intrapartum HIV-1 transmission, and then built sequentially on previous results to improve approaches to the prevention of mother-to-child transmission of HIV-1 in resourcelimited settings. The World Health Organization (WHO) guidelines for prevention evolved as the results from such clinical trials became available.

With the increasing global availability of antiretroviral drugs, there has also been a convergence of guidelines for prevention and treatment in resource-rich countries and the WHO guidelines for resource-limited countries. Moreover, recent studies have shown that it is possible to substantially reduce the size of the latent reservoir in infected children with very early treatment. Continued progress towards eliminating pediatric HIV-1 infection requires finding solutions to long-standing problems in maternal and child health systems in countries with limited resources so as to improve the delivery of preventive health care services at each stage of gestation, delivery, and breast-feeding during which transmission from mother to child may occur. These problems include inadequate access to early antenatal care, poor linkage between mother–child pairs and postnatal health services, and a lack of systems to ensure longterm retention in care and continued provision of and adherence to maternal antiretroviral therapy. The achievement of remission, and potentially the cure, of pediatric HIV-1 infection will require additional research to improve both methods of early diagnosis in resource-limited settings and methods to define the size and distribution of the latent HIV-1 reservoir in children more accurately. New antiretroviral drugs that are highly active, palatable, and inexpensive are needed for pediatric treatment, as are improved systems for providing children with access to lifesaving antiretroviral therapies.

13. TMIH 2016:21(3):373-84. Epub 2016 Jan 22

Anaemia in HIV-infected pregnant women receiving triple antiretroviral combination therapy for prevention of mother-to-child transmission: a secondary analysis of the Kisumu breastfeeding study (KiBS)

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Objective: The prevalence of anaemia during pregnancy is estimated to be 35-75% in sub-Saharan Africa and is associated with an increased risk of maternal mortality. We evaluated the frequency and factors associated with anaemia in HIV-infected women undergoing antiretroviral (ARV) therapy for prevention of mother-to-child transmission (PMTCT) enrolled in The Kisumu Breastfeeding Study 2003-2009.
Methods: Maternal haematological parameters were monitored from 32 to 34 weeks of gestation to 2 years post-delivery among 522 enrolled women. Clinical and laboratory assessments for causes of anaemia were performed, and appropriate management was initiated. Anaemia was graded using the National Institutes of Health Division of AIDS 1994 Adult Toxicity Tables. Data were analysed using SAS software, v 9.2. The Wilcoxon two-sample rank test was used to compare groups. A logistic regression model was fitted to describe the trend in anaemia over time.
Results: At enrolment, the prevalence of any grade anaemia (Hb < 9.4 g/dl) was 61.8%, but fell during ARV therapy, reaching a nadir (7.4%) by 6 months post-partum. A total of 41 women (8%) developed severe anaemia (Hb < 7 g/dl) during follow-up; 2 (4.9%) were hospitalised for blood transfusion, whereas 3 (7.3%) were transfused while hospitalised (for delivery). The greatest proportion of severe anaemia events occurred around delivery (48.8%; n = 20). Anaemia (Hb ≥ 7 and < 9.4 g/dl) at enrolment was associated with severe anaemia at delivery (OR 5.87; 95% CI: 4.48, 7.68, P < 0.01). Few cases of severe anaemia coincided with clinical malaria (24.4%; n = 10) and helminth (7.3%; n = 3) infections.
Conclusion: Resolution of anaemia among most participants during study follow-up was likely related to receipt of ARV therapy. Efforts should be geared towards addressing common causes of anaemia in HIV-infected pregnant women, prioritising initiation of ARV therapy and management of peripartum blood loss.

14. TMIH 2016;21(4):479-85. Epub 2016 Feb 29

Lost opportunities to identify and treat HIV-positive patients: results from a baseline assessment of provider-initiated HIV testing and counselling (PITC) in Malawi
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Objective: To assess implementation of provider-initiated testing and counselling (PITC) for HIV in Malawi.
Methods: A review of PITC practices within 118 departments in 12 Ministry of Health (MoH) facilities across Malawi was conducted. Information on PITC practices was collected via a health facility survey. Data describing patient visits and HIV tests were abstracted from routinely collected programme data.
Results: Reported PITC practices were highly variable. Most providers practiced symptom-based PITC. Antenatal clinics and maternity wards reported widespread use of routine opt-out PITC. In 2014, there was approximately 1 HIV test for every 15 clinic visits. HIV status was ascertained in 94.3% (5293/5615) of patients at tuberculosis clinics, 92.6% (30 675/33 142) of patients at antenatal clinics and 49.4% (6871/13 914) of patients at sexually transmitted infection clinics. Reported challenges to delivering PITC included test kit shortages (71/71 providers), insufficient physical space (58/71) and inadequate number of HIV counsellors (32/71) while providers from inpatient units cited the inability to test on weekends.
Conclusions: Various models of PITC currently exist at MoH facilities in Malawi. Only antenatal and maternity clinics demonstrated high rates of routine opt-out PITC. The low ratio of facility visits to HIV tests suggests missed opportunities for HIV testing. However, the high proportion of patients at TB and antenatal clinics with known HIV status suggests that routine PITC is feasible. These results underscore the need to develop clear, standardised PITC policy and protocols, and to address obstacles of limited health commodities, infrastructure and human resources.

Malaria

15. **Am J TMH 2016;94(4):868-78. Epub 2016 Feb 1**

Eave Screening and Push-Pull Tactics to Reduce House Entry by Vectors of Malaria
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Long-lasting insecticidal nets and indoor residual spraying have contributed to a decline in malaria over the last decade, but progress is threatened by the development of physiological and behavioral resistance of mosquitoes against insecticides. Acknowledging the need for alternative vector control tools, we quantified the effects of eave screening in combination with a push-pull system based on the simultaneous use of a repellent (push) and attractant-baited traps (pull). Field experiments in western Kenya showed that eave screening, whether used in combination with an attractant-baited trap or not, was highly effective in reducing house entry by malaria mosquitoes. The magnitude of the effect varied for different mosquito species and between two experiments, but the reduction in house entry was always considerable (between 61% and 99%). The use of outdoor, attractant-baited traps alone did not have a significant impact on mosquito house entry but the high number of mosquitoes trapped outdoors indicates that attractant-baited traps could be used for removal trapping, which would enhance outdoor as well as indoor protection against mosquito bites. As eave screening was effective by itself, addition of a repellent was of limited value. Nevertheless, repellents may play a role in reducing outdoor malaria transmission in the peridomestic area.

16. **NEJM 2016;374:913-927**

Four Artemisinin-Based Treatments in African Pregnant Women with Malaria
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Background: Information regarding the safety and efficacy of artemisinin combination treatments for malaria in pregnant women is limited, particularly among women who live in sub-Saharan Africa.
Methods: We conducted a multicenter, randomized, open-label trial of treatments for malaria in pregnant women in four African countries. A total of 3428 pregnant women in the second or third trimester who had falciparum malaria (at any parasite density and regardless of symptoms) were treated with artemether–lumefantrine, amodiaquine–artesunate, mefloquine–artesunate, or dihydroartemisinin–piperaquine. The primary end points were the polymerase-chain-reaction (PCR)–adjusted cure rates (i.e., cure of the original infection; new infections during follow-up were not considered to be treatment failures) at day 63 and safety outcomes.
Results: The PCR-adjusted cure rates in the per-protocol analysis were 94.8% in the artemether–lumefantrine group, 98.5% in the amodiaquine–artesunate group, 99.2% in the dihydroartemisinin–piperaquine group, and 96.8% in the mefloquine–artesunate group; the PCR-adjusted cure rates in the intention-to-treat analysis were 94.2%, 96.9%, 98.0%, and 95.5%, respectively. There was no significant difference among the amodiaquine–artesunate group, dihydroartemisinin–piperaquine group, and the mefloquine–artesunate group. The cure rate in the artemether–lumefantrine group was significantly lower than that in the other three groups, although the absolute difference was within the 5-percentage-point margin for equivalence. The unadjusted cure rates, used as a measure of the post-treatment prophylactic effect, were significantly lower in the artemether–lumefantrine group (52.5%) than in groups that received amodiaquine–artesunate (82.3%), dihydroartemisinin–piperaquine (86.9%), or mefloquine–artesunate (73.8%). No significant difference in the rate of serious adverse events and in birth outcomes was found among the treatment groups. Drug-related adverse events such as asthenia, poor appetite, dizziness, nausea, and vomiting occurred significantly more frequently in the mefloquine–artesunate group (50.6%) and the amodiaquine–artesunate group (48.5%) than in the dihydroartemisinin–piperaquine group (20.6%) and the artemether–lumefantrine group (11.5%) ($P<0.001$ for comparison among the four groups).
Conclusions: Artemether–lumefantrine was associated with the fewest adverse effects and with acceptable cure rates but provided the shortest post-treatment prophylaxis, whereas dihydroartemisinin–piperaquine had the best efficacy and an acceptable safety profile.

17. PLoS Med (2016);13(2): e1001964

Mortality, Morbidity, and Developmental Outcomes in Infants Born to Women Who Received Either Mefloquine or Sulfadoxine-Pyrimethamine as Intermittent Preventive Treatment of Malaria in Pregnancy: A Cohort Study

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Background: Little is known about the effects of intermittent preventive treatment of malaria in pregnancy (IPTp) on the health of sub-Saharan African infants. We have evaluated the safety of IPTp with mefloquine (MQ) compared to sulfadoxine-pyrimethamine (SP) for important infant health and developmental outcomes.

Methods and Findings: In the context of a multicenter randomized controlled trial evaluating the safety and efficacy of IPTp with MQ compared to SP in pregnancy carried out in four sub-Saharan countries (Mozambique, Benin, Gabon, and Tanzania), 4,247 newborns, 2,815 born to women who received MQ and 1,432 born to women who received SP for IPTp, were followed up until 12 mo of age. Anthropometric parameters and psychomotor development were assessed at 1, 9, and 12 mo of age, and the incidence of malaria, anemia, hospital admissions, outpatient visits, and mortality were determined until 12 mo of age. No significant differences were found in the proportion of infants with stunting, underweight, wasting, and severe acute malnutrition at 1, 9, and 12 mo of age between infants born to women who were on IPTp with MQ versus SP. Except for three items evaluated at 9 mo of age, no significant differences were observed in the psychomotor development milestones assessed. Incidence of malaria, anemia, hospital admissions, outpatient visits, and mortality were similar between the two groups. Information on the outcomes at 12 mo of age was unavailable in 26% of the infants, 761 (27%) from the MQ group and 377 (26%) from the SP group. Reasons for not completing the study were death (4% of total study population), study withdrawal (6%), migration (8%), and loss to follow-up (9%).

Conclusions: No significant differences were found between IPTp with MQ and SP administered in pregnancy on infant mortality, morbidity, and nutritional outcomes. The poorer performance on certain psychomotor development milestones at 9 mo of age in children born to women in the MQ group compared to those in the SP group may deserve further studies.

Mother and Child Health

18. BMJ 2016;352:i1473, Feature Mother and child health

The global push for institutional childbirths—in unhygienic facilities

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Healthcare facilities offer professional assistance to women giving birth, writes Jocalyn Clark, but many in developing countries are filthy, lacking clean water and sanitation

Increasing and regularly monitoring the number of women giving birth in institutions has been central to international strategies to improve the health of mothers and babies in the developing world. In India, the $200m (£141m; €184m) a year Janani Suraksha Yojana programme pays women to give birth in healthcare facilities rather than at home, as is tradition. Bangladesh and Nepal have similar conditional cash transfer programmes.

This push has largely neglected a sad irony: in much of the developing world, where 99% of maternal and newborn deaths occur, hospitals and other healthcare facilities are in a poor state.

In an unprecedented analysis of water, sanitation, and hygiene (WASH) in healthcare facilities in low income countries, the World Health Organisation recently reported that 38% have no decent water source.This leaves doctors, nurses, and midwives struggling to care for patients—and WHO

“embarrassed.” One fifth of facilities surveyed in 54 countries had inadequate sanitation, and 35% lacked water and soap for healthcare providers and patients to wash their hands.
Mother and baby risk infection
Poor hygiene is of special concern in labour wards, said Wendy Graham, a maternal mortality expert from the University of Aberdeen who is raising awareness of WASH. In dirty conditions, mother and baby risk infections from many sources, she said.
Infection may be introduced to the genital tract during delivery from poor hand hygiene or contaminated surfaces, which can lead to death from puerperal sepsis. When dirty hands, surfaces, or blades are used, wounds from cutting the umbilical cord, perineal tears, and caesarean section introduce routes of transmission of infection.

19. Lancet 2016;387(10017):462-74

Global, regional, and national levels and trends in maternal mortality between 1990 and 2015, with scenario-based projections to 2030: a systematic analysis by the UN Maternal Mortality Estimation Inter-Agency Group
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Background: Millennium Development Goal 5 calls for a 75% reduction in the maternal mortality ratio (MMR) between 1990 and 2015. We estimated levels and trends in maternal mortality for 183 countries to assess progress made. Based on MMR estimates for 2015, we constructed projections to show the requirements for the Sustainable Development Goal (SDG) of less than 70 maternal deaths per 100,000 livebirths globally by 2030.
Methods: We updated the UN Maternal Mortality Estimation Inter-Agency Group (MMEIG) database with more than 200 additional records (vital statistics from civil registration systems, surveys, studies, or reports). We generated estimates of maternal mortality and related indicators with 80% uncertainty intervals (UIs) using a Bayesian model. The model combines the rate of change implied by a multilevel regression model with a time-series model to capture data-driven changes in country-specific MMRs, and includes a data model to adjust for systematic and random errors associated with different data sources.
Results: We had data for 171 of 183 countries. The global MMR fell from 385 deaths per 100,000 livebirths (80% UI 359-427) in 1990, to 216 (207-249) in 2015, corresponding to a relative decline of 43·9% (34·0-48·7), with 303,000 (291,000-349,000) maternal deaths worldwide in 2015. Regional progress in reducing the MMR since 1990 ranged from an annual rate of reduction of 1·8% (0·0-3·1) in the Caribbean to 5·0% (4·0-6·0) in eastern Asia. Regional MMRs for 2015 ranged from 12 deaths per 100,000 livebirths (11-14) for high-income regions to 546 (511-652) for sub-Saharan Africa. Accelerated progress will be needed to achieve the SDG goal; countries will need to reduce their MMRs at an annual rate of reduction of at least 7·5%.
Interpretation: Despite global progress in reducing maternal mortality, immediate action is needed to meet the ambitious SDG 2030 target, and ultimately eliminate preventable maternal mortality. Although the rates of reduction that are needed to achieve country-specific SDG targets are ambitious for most high mortality countries, countries that made a concerted effort to reduce maternal mortality between 2000 and 2010 provide inspiration and guidance on how to accomplish the acceleration necessary to substantially reduce preventable maternal deaths.
Funding: National University of Singapore, National Institute of Child Health and Human Development, USAID, and the UNDP/UNFPA/UNICEF/WHO/World Bank Special Programme of Research, Development and Research Training in Human Reproduction.

20. Lancet 2016;387(10017):475-90

Breastfeeding in the 21st century: epidemiology, mechanisms, and lifelong effect
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The importance of breastfeeding in low-income and middle-income countries is well recognised, but less consensus exists about its importance in high-income countries. In low-income and middle-income countries, only 37% of children younger than 6 months of age are exclusively breastfed. With few exceptions, breastfeeding duration is shorter in high-income countries than in those that are resource-poor. Our meta-analyses indicate protection against child infections and malocclusion, increases in intelligence, and probable reductions in overweight and diabetes. We did not find associations with allergic disorders such as asthma or with blood pressure or cholesterol, and we noted an increase in tooth decay with longer periods of breastfeeding. For nursing women, breastfeeding gave protection against breast cancer and it improved birth spacing, and it might also protect against ovarian cancer and type 2 diabetes. The scaling up of breastfeeding to a near universal level could prevent 823,000 annual deaths in children younger than 5 years and 20,000 annual deaths from breast cancer. Recent epidemiological and biological findings from during the past decade expand on the known benefits of breastfeeding for women and children, whether they are rich or poor.

21. Lancet 2016;387(10019):703-16. Epub 2016 Jan 19

Stillbirths: ending preventable deaths by 2030 Series
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Efforts to achieve the new worldwide goals for maternal and child survival will also prevent stillbirth and improve health and developmental outcomes. However, the number of annual stillbirths remains unchanged since 2011 and is unacceptably high: an estimated 2.6 million in 2015. Failure to consistently include global targets or indicators for stillbirth in post-2015 initiatives shows that stillbirths are hidden in the worldwide agenda. This Series paper summarises findings from previous papers in this Series, presents new analyses, and proposes specific criteria for successful integration of stillbirths into post-2015 initiatives for women's and children's health. Five priority areas to change the stillbirth trend include intentional leadership; increased voice, especially of women; implementation of integrated interventions with commensurate investment; indicators to measure effect of interventions and especially to monitor progress; and investigation into crucial knowledge gaps. The post-2015 agenda represents opportunities for all stakeholders to act together to end all preventable deaths, including stillbirths.
Other titles in the series
Stillbirths: progress and unfinished business J Frederik Frøen, et al
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Stillbirths: economic and psychosocial consequences Alexander E P Heazell, et al
Stillbirths: recall to action in high-income countries Vicki Flenady, et al
Stillbirths: ending preventable deaths by 2030 Luc de Bernis, et al

22. PLoS Med 2016;13(2): e1001951

Effect of Short-Term Supplementation with Ready-to-Use Therapeutic Food or Micronutrients for Children after Illness for Prevention of Malnutrition: A Randomised Controlled Trial in Uganda.
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Background: Globally, Médecins Sans Frontières (MSF) treats more than 300,000 severely malnourished children annually. Malnutrition is not only caused by lack of food but also by illnesses and by poor infant and child feeding practices. Breaking the vicious cycle of illness and malnutrition by providing ill children with nutritional supplementation is a potentially powerful strategy for preventing malnutrition that has not been adequately investigated. Therefore, MSF investigated

whether incidence of malnutrition among ill children <5 y old could be reduced by providing a fortified food product or micronutrients during their 2-wk convalescence period. Two trials, one in Nigeria and one in Uganda, were conducted; here, we report on the trial that took place in Kaabong, a poor agropastoral region of Karamoja, in east Uganda. While the region of Karamoja shows an acute malnutrition rate between 8.4% and 11.5% of which 2% to 3% severe malnutrition, more than half (58%) of the population in the district of Kaabong is considered food insecure.

Methods and Findings: We investigated the effect of two types of nutritional supplementation on the incidence of malnutrition in ill children presenting at outpatient clinics during March 2011 to April 2012 in Kaabong, Karamoja region, Uganda, a resource-poor region where malnutrition is a chronic problem for its seminomadic population. A three-armed, partially-blinded, randomised controlled trial was conducted in children diagnosed with malaria, diarrhoea, or lower respiratory tract infection. Non-malnourished children aged 6 to 59 mo were randomised to one of three arms: one sachet/d of ready-to-use therapeutic food (RUTF), two sachets/d of micronutrient powder (MNP), or no supplement (control) for 14 d for each illness over 6 mo. The primary outcome was the incidence of first negative nutritional outcome (NNO) during the 6 mo follow-up. NNO was a study-specific measure used to indicate progression to moderate or severe acute malnutrition; it was defined as weight-for-height z-score <−2, mid-upper arm circumference (MUAC) <115 mm, or oedema, whichever came first.

Of the 2,202 randomised participants, 51.2% were girls, and the mean age was 25.2 (±13.8) mo; 148 (6.7%) participants were lost to follow-up, 9 (0.4%) died, and 14 (0.6%) were admitted to hospital. The incidence rates of NNO (first event/year) for the RUTF, MNP, and control groups were 0.143 (95% confidence interval [CI], 0.107–0.191), 0.185 (0.141–0.239), and 0.213 (0.167–0.272), respectively. The incidence rate ratio was 0.67 (95% CI, 0.46–0.98; p = 0.037) for RUTF versus control; a reduction of 33.3%. The incidence rate ratio was 0.86 (0.61–1.23; p = 0.413) for MNP versus control and 0.77 for RUTF versus MNP (95% CI 0.52–1.15; p= 0.200). The average numbers of study illnesses for the RUTF, MNP, and control groups were 2.3 (95% CI, 2.2–2.4), 2.1 (2.0–2.3), and 2.3 (2.2–2.5). The proportions of children who died in the RUTF, MNP, and control groups were 0%, 0.8%, and 0.4%.

The findings apply to ill but not malnourished children and cannot be generalised to a general population including children who are not necessarily ill or who are already malnourished.

Conclusions: A 2-wk nutrition supplementation programme with RUTF as part of routine primary medical care to non-malnourished children with malaria, LRTI, or diarrhoea proved effective in preventing malnutrition in eastern Uganda. The low incidence of malnutrition in this population may warrant a more targeted intervention to improve cost effectiveness.

23. PLoS Med 2016;13(2): e1001952

Effect of Short-Term Supplementation with Ready-to-Use Therapeutic Food or Micronutrients for Children after Illness for Prevention of Malnutrition: A Randomised Controlled Trial in Nigeria.

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Background: Globally, Médecins Sans Frontières (MSF) treats more than 300,000 severely malnourished children annually. Malnutrition is not only caused by lack of food and poor infant and child feeding practices but also by illnesses. Breaking the vicious cycle of illness and malnutrition by providing ill children with nutritional supplementation is a potentially powerful strategy for preventing malnutrition that has not been adequately investigated. Therefore, MSF investigated whether incidence of malnutrition among ill children <5 y old could be reduced by providing a fortified food product or micronutrients during their 2-wk convalescence period. Two trials, one in Nigeria and one in Uganda, were conducted; here we report on the trial that took place in Goronyo, a rural region of northwest Nigeria with high morbidity and malnutrition rates.

Methods and Findings: We investigated the effect of supplementation with ready-to-use therapeutic food (RUTF) and a micronutrient powder (MNP) on the incidence of malnutrition in ill children

presenting at an outpatient clinic in Goronyo during February to September 2012. A three-armed, partially-blinded, randomised controlled trial was conducted in children diagnosed as having malaria, diarrhoea, or lower respiratory tract infection. Children aged 6 to 59 mo were randomised to one of three arms: one sachet/d of RUTF; two sachets/d of micronutrients or no supplement (control) for 14 d for each illness over 6 mo. The primary outcome was the incidence of first negative nutritional outcome (NNO) during the 6 mo follow-up. NNO was a study-specific measure used to indicate occurrence of malnutrition; it was defined as low weight-for-height z-score (<−2 for non-malnourished and <−3 for moderately malnourished children), mid-upper arm circumference <115 mm, or oedema, whichever came first.
Of the 2,213 randomised participants, 50.0% were female and the mean age was 20.2 (standard deviation 11.2) months; 160 (7.2%) were lost to follow-up, 54 (2.4%) were admitted to hospital, and 29 (1.3%) died. The incidence rates of NNO for the RUTF, MNP, and control groups were 0.522 (95% confidence interval (95% CI), 0.442–0.617), 0.495 (0.415–0.589), and 0.566 (0.479–0.668) first events/y, respectively. The incidence rate ratio was 0.92 (95% CI, 0.74–1.15; p = 0.471) for RUTF versus control; 0.87 (0.70–1.10; p = 0.242) for MNP versus control and 1.06 (0.84–1.33, p = 0.642) for RUTF versus MNP. A subgroup analysis showed no interaction nor confounding, nor a different effectiveness of supplementation, among children who were moderately malnourished compared with non-malnourished at enrollment. The average number of study illnesses for the RUTF, MNP, and control groups were 4.2 (95% CI, 4.0–4.3), 3.4 (3.2–3.6), and 3.6 (3.4–3.7). The proportion of children who died in the RUTF, MNP, and control groups were 0.8% (95% CI, 0.3–1.8), 1.8% (1.0–3.3), and 1.4% (0.7–2.8).
Conclusions: A 2-wk supplementation with RUTF or MNP to ill children as part of routine primary medical care did not reduce the incidence of malnutrition. The lack of effect in Goronyo may be due to a high frequency of morbidity, which probably further affects a child's nutritional status and children's ability to escape from the illness–malnutrition cycle. The duration of the supplementation may have been too short or the doses of the supplements may have been too low to mitigate the effects of high morbidity and pre-existing malnutrition. An integrated approach combining prevention and treatment of diseases and treatment of moderate malnutrition, rather than prevention of malnutrition by nutritional supplementation alone, might be more effective in reducing the incidence of acute malnutrition in ill children.

24. PLoS Med 2016;13(2): e1001962

A Time for Global Action: Addressing Girls' Menstrual Hygiene Management Needs in Schools
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Summary Points

- There is an absence of guidance, facilities, and materials for schoolgirls to manage their menstruation in low- and middle-income countries (LMICs).
- Formative evidence has raised awareness that poor menstrual hygiene management (MHM) contributes to inequity, increasing exposure to transactional sex to obtain sanitary items, with some evidence of an effect on school indicators and with repercussions for sexual, reproductive, and general health throughout the life course.
- Despite increasing evidence and interest in taking action to improve school conditions for girls, there has not been a systematic mapping of MHM priorities or coordination of relevant sectors and disciplines to catalyze change, with a need to develop country-level expertise.
- Columbia University and the United Nations Children's Fund (UNICEF) convened members of academia, nongovernmental organizations, the UN, donor agencies, the private sector, and

social entrepreneurial groups in October 2014 (“MHM in Ten”) to identify key public health issues requiring prioritization, coordination, and investment by 2024.

- Five key priorities were identified to guide global, national, and local action to achieve this vision by 2024.

25. PLoS Med 2016;13(3): e1001972

Length of Stay After Childbirth in 92 Countries and Associated Factors in 30 Low- and Middle-Income Countries: Compilation of Reported Data and a Cross-sectional Analysis from Nationally Representative Surveys
Campbell OMR, et al., Faculty of Epidemiology and Population Health, London School of Hygiene & Tropical Medicine, London, UK <oona.campbell@lshtm.ac.uk>

Background: Following childbirth, women need to stay sufficiently long in health facilities to receive adequate care. Little is known about length of stay following childbirth in low- and middle-income countries or its determinants.
Methods and Findings: We described length of stay after facility delivery in 92 countries. We then created a conceptual framework of the main drivers of length of stay, and explored factors associated with length of stay in 30 countries using multivariable linear regression. Finally, we used multivariable logistic regression to examine the factors associated with stays that were “too short” (<24 h for vaginal deliveries and <72 h for cesarean-section deliveries).
Across countries, the mean length of stay ranged from 1.3 to 6.6 d: 0.5 to 6.2 d for singleton vaginal deliveries and 2.5 to 9.3 d for cesarean-section deliveries. The percentage of women staying too short ranged from 0.2% to 83% for vaginal deliveries and from 1% to 75% for cesarean-section deliveries. Our conceptual framework identified three broad categories of factors that influenced length of stay: need-related determinants that required an indicated extension of stay, and health-system and woman/family dimensions that were drivers of inappropriately short or long stays. The factors identified as independently important in our regression analyses included cesarean-section delivery, birthweight, multiple birth, and infant survival status. Older women and women whose infants were delivered by doctors had extended lengths of stay, as did poorer women. Reliance on factors captured in secondary data that were self-reported by women up to 5 y after a live birth was the main limitation.
Conclusions: Length of stay after childbirth is very variable between countries. Substantial proportions of women stay too short to receive adequate postnatal care. We need to ensure that facilities have skilled birth attendants and effective elements of care, but also that women stay long enough to benefit from these. The challenge is to commit to achieving adequate lengths of stay in low- and middle-income countries, while ensuring any additional time is used to provide high-quality and respectful care.

26. TMIH 2016;21(4):486-503. Epub 2016 Mar 7

Family planning, antenatal and delivery care: cross-sectional survey evidence on levels of coverage and inequalities by public and private sector in 57 low- and middle-income countries
Campbell OMR, et al., Faculty of Epidemiology and Population Health, London School of Hygiene & Tropical Medicine, London, UK <oona.campbell@lshtm.ac.uk>

Objective: The Objective of this study was to assess the role of the private sector in low- and middle-income countries (LMICs). We used Demographic and Health Surveys for 57 countries (2000-2013) to evaluate the private sector's share in providing three reproductive and maternal/newborn health services (family planning, antenatal and delivery care), in total and by socio-economic position.
Methods: We used data from 865 547 women aged 15-49, representing a total of 3 billion people. We defined 'met and unmet need for services' and 'use of appropriate service types' clearly and developed explicit classifications of source and sector of provision.

Results: Across the four regions (sub-Saharan Africa, Middle East/Europe, Asia and Latin America), unmet need ranged from 28% to 61% for family planning, 8% to 22% for ANC and 21% to 51% for delivery care. The private-sector share among users of family planning services was 37-39% across regions (overall mean: 37%; median across countries: 41%). The private-sector market share among users of ANC was 13-61% across regions (overall mean: 44%; median across countries: 15%). The private-sector share among appropriate deliveries was 9-56% across regions (overall mean: 40%; median across countries: 14%). For all three healthcare services, women in the richest wealth quintile used private services more than the poorest. Wealth gaps in met need for services were smallest for family planning and largest for delivery care.
Conclusions: The private sector serves substantial numbers of women in LMICs, particularly the richest. To achieve universal health coverage, including adequate quality care, it is imperative to understand this sector, starting with improved data collection on healthcare provision.

27. TMIH 2016;21(4):525-34. Epub 2016 Mar 4

Criteria-based audit of caesarean section in a referral hospital in rural Tanzania
Heemelaar S, Nelissen E, Mdoe P, et al.
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Objective: WHO uses the Caesarean section (CS) rate to monitor implementation of emergency obstetric care (EmOC). Although CS rates are rising in sub-Saharan Africa, maternal outcome has not improved. We audited indications for CS and related complications among women with severe maternal morbidity and mortality in a referral hospital in rural Tanzania.
Methods: Cross-sectional study was from November 2009 to November 2011. Women with severe maternal morbidity and mortality were identified and those with CS were included in this audit. Audit criteria were developed based on the literature review and (inter)national guidelines. Tanzanian and Dutch doctors reviewed hospital notes. The main outcome measured was prevalence of substandard quality of care leading to unnecessary CS and delay in performing interventions to prevent CS.
Results: A total of 216 maternal near misses and 32 pregnancy-related deaths were identified, of which 82 (33.1%) had a CS. Indication for CS was in accordance with audit criteria for 36 of 82 (44.0%) cases without delay. In 20 of 82 (24.4%) cases, the indication was correct; however, there was significant delay in providing standard obstetric care. In 16 of 82 (19.5%) cases, the indication for CS was not in accordance with audit criteria. During office hours, CS was more often correctly indicated than outside office hours (60.0% vs. 36.0%, $P < 0.05$).
Discussion: Caesarean section rate is not an useful indicator to monitor quality of EmOC as a high rate of unnecessary and potentially preventable CS was identified in this audit.

28. TMIH 2016;21(4):535-45. Epub 2016 Mar 4

Characteristics of neonatal near miss in hospitals in Benin, Burkina Faso and Morocco in 2012-2013
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Objective: The Objective of this study is to explore the usefulness of neonatal near miss in low- and middle-income countries by examining the incidence of neonatal near miss and pre-discharge neonatal deaths across various obstetric risk categories in 17 hospitals in Benin, Burkina Faso and Morocco.
Methods: Data were collected on all maternal deaths, maternal near miss, neonatal near miss (based on organ-dysfunction markers), Caesarean sections, stillbirths, neonatal deaths before discharge and non-cephalic presentations, and on a sample of births not falling in any of the above categories.
Results: The burden of stillbirth, pre-discharge neonatal death or neonatal near miss ranged from 23 to 129 per 1000 births in Moroccan and Beninese hospitals, respectively. Perinatal deaths (range 17-89 per 1000 births) were more common than neonatal near miss (range 6-43 per 1000 live births), and between a fifth and a third of women who had suffered a maternal near miss lost their baby. Pre-

discharge neonatal deaths and neonatal near miss had a similar distribution of markers of organ dysfunction, but unlike pre-discharge neonatal deaths most neonatal near miss (63%, 81% and 71% in Benin, Burkina Faso and Morocco, respectively) occurred among babies who were not considered premature, low birthweight or with a low 5-min Apgar score as defined by WHO's pragmatic markers of severe neonatal morbidity.
Conclusion: Whether the measurement of neonatal near miss adds useful insights into the quality of perinatal or newborn care in settings where facility-based intrapartum and early newborn mortality is very high is uncertain. Perhaps the greatest advantage of adding near miss is the shift in focus from failure to success so that lessons can be learned on how to save lives even when clinical conditions are life-threatening.

29. TMIH 2016;21(4):504-14. Epub 2016 Feb 17

Why women bypass front-line health facility services in pursuit of obstetric care provided elsewhere: a case study in three rural districts of Tanzania
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Objectives: In the Tanzanian health system, women are expected to first visit their nearest front-line health facility (FLF) for delivery. However, women frequently bypass these FLF. Our study estimates the extent of bypassing for childbirth and assesses factors associated with this behaviour.
Methods: Data describing the experiences of 597 women who recently delivered at a facility and the EmONC service capability at 107 health facilities were collected in 2011. Women who did not deliver at their nearest FLF were considered 'bypassers'. Factors associated with bypassing were assessed using multivariate logistic regression models. Three sets of analyses were conducted: among 597 women who delivered at the first facility they visited, among 521 women with no previous complications, and among 407 women not primigravida and without previous complications.
Results: More than 75.4% of women bypassed. In the fully adjusted model of all 597 women those who had experienced complications were more likely to bypass for delivery [OR = 6.31 (2.36, 16.86)]. In the fully adjusted model excluding women with previous complications, primigravida women were more likely to bypass [OR = 3.70 (1.71, 8.01)]. Fully adjusted models for each set of analysis found that, for each additional emergency obstetric and newborn care signal function (EmONC SF) available at the nearest FLF, women's odds of bypassing almost halved.
Conclusions: Bypassing is highly associated with EmONC SF score at nearest FLF, controlling for individual and community-level factors.

NCD

30. Am J TMH 2016;Feb 15. pii: 15-0715. [Epub ahead of print]

An Emerging Epidemic of Noncommunicable Diseases in Developing Populations Due to a Triple Evolutionary Mismatch
Koopman JJ, van Bodegom D, Ziem JB, et al. Leiden University Medical Center.

With their transition from adverse to affluent environments, developing populations experience a rapid increase in the number of individuals with noncommunicable diseases. Here, we emphasize that developing populations are more susceptible than western populations to acquire these chronic diseases, because their genetic, cultural, and epigenetic characteristics do not match with the eagerly awaited affluent environments. In regard to this, there is an urgent need for public health organizations to reorganize current environments in developing populations so as to fit their inherited characteristics. Unfortunately, this need is neglected as an essential part of the Sustainable Development Goals that form the core of the United Nations' Post-2015 Development Agenda. Only through global

collaborative efforts can the environments in developing populations be reorganized and, thereby, the emerging epidemic of noncommunicable diseases be stalled.

31. **Lancet 2016;Apr 5. pii: S0140-6736(16)00618-8. [Epub ahead of print]**

Worldwide trends in diabetes since 1980: a pooled analysis of 751 population-based studies with 4·4 million participants
NCD Risk Factor Collaboration (NCD-RisC)

Background: One of the global targets for non-communicable diseases is to halt, by 2025, the rise in the age-standardised adult prevalence of diabetes at its 2010 levels. We aimed to estimate worldwide trends in diabetes, how likely it is for countries to achieve the global target, and how changes in prevalence, together with population growth and ageing, are affecting the number of adults with diabetes.
Methods: We pooled data from population-based studies that had collected data on diabetes through measurement of its biomarkers. We used a Bayesian hierarchical model to estimate trends in diabetes prevalence-defined as fasting plasma glucose of 7·0 mmol/L or higher, or history of diagnosis with diabetes, or use of insulin or oral hypoglycaemic drugs-in 200 countries and territories in 21 regions, by sex and from 1980 to 2014. We also calculated the posterior probability of meeting the global diabetes target if post-2000 trends continue.
Findings: We used data from 751 studies including 4 372 000 adults from 146 of the 200 countries we make estimates for. Global age-standardised diabetes prevalence increased from 4·3% (95% credible interval 2·4-7·0) in 1980 to 9·0% (7·2-11·1) in 2014 in men, and from 5·0% (2·9-7·9) to 7·9% (6·4-9·7) in women. The number of adults with diabetes in the world increased from 108 million in 1980 to 422 million in 2014 (28·5% due to the rise in prevalence, 39·7% due to population growth and ageing, and 31·8% due to interaction of these two factors). Age-standardised adult diabetes prevalence in 2014 was lowest in northwestern Europe, and highest in Polynesia and Micronesia, at nearly 25%, followed by Melanesia and the Middle East and north Africa. Between 1980 and 2014 there was little change in age-standardised diabetes prevalence in adult women in continental western Europe, although crude prevalence rose because of ageing of the population. By contrast, age-standardised adult prevalence rose by 15 percentage points in men and women in Polynesia and Micronesia. In 2014, American Samoa had the highest national prevalence of diabetes (>30% in both sexes), with age-standardised adult prevalence also higher than 25% in some other islands in Polynesia and Micronesia. If post-2000 trends continue, the probability of meeting the global target of halting the rise in the prevalence of diabetes by 2025 at the 2010 level worldwide is lower than 1% for men and is 1% for women. Only nine countries for men and 29 countries for women, mostly in western Europe, have a 50% or higher probability of meeting the global target.
Interpretation: Since 1980, age-standardised diabetes prevalence in adults has increased, or at best remained unchanged, in every country. Together with population growth and ageing, this rise has led to a near quadrupling of the number of adults with diabetes worldwide. The burden of diabetes, both in terms of prevalence and number of adults affected, has increased faster in low-income and middle-income countries than in high-income countries.

32. **PLoS Med 2016;13(3): e1001986**

Editorial. Pragmatic Trials for Noncommunicable Diseases: Relieving Constraints
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At the 65th World Health Assembly in 2012, all World Health Organization member states made a historic commitment to reduce premature deaths from noncommunicable diseases (NCDs, including cardiovascular diseases, diabetes, cancer, and chronic respiratory diseases) by 25% by 2025. Subsequently, the World Health Assembly in 2013 agreed to adopt a global monitoring framework that included nine ambitious global NCD targets for 2025. These targets address key risk factors including tobacco and alcohol use, physical inactivity, high salt intake, high blood pressure, diabetes, and obesity and also the availability of basic technologies and medicines for the prevention and treatment of major NCDs. Many of these targets reflect the fact that a wide range of safe and effective

treatments for the prevention and management of many NCDs already exists. These treatments have been the product of decades of "discovery research" utilising high-quality, large-scale randomised controlled trials to produce reliable evidence of safety and efficacy. Unfortunately, translation of these important discoveries has been less than optimal globally, but particularly so in low- and middle-income countries that are now bearing the brunt of the global NCD burden. This translation gap is fuelled by uncertainty about how best to implement effective treatments tested under ideal conditions into the complex and often resource-constrained systems in which they need to be delivered.
Clear demonstration of such knowledge translation gaps has raised the profile of implementation research in NCD prevention and control.
One method is the pragmatic randomised controlled trial (pRCT), important to answer questions about whether there is a high probability that a particular intervention will produce an expected outcome in a particular context. Unlike "discovery" research, which is primarily designed to determine the safety and efficacy of an intervention under ideal conditions, pRCTs aim to reflect effectiveness of strategies to utilise such interventions under "real world" conditions.

For NCDs, pRCTs are important to identify the best way to implement the plethora of available effective preventive interventions. If current constraints are not addressed, meeting many of the 2025 voluntary goals for NCD control may be even more challenging.

33. TMIH 2016;21(3):417-26. doi: 10.1111/tmi.12652. Epub 2016 Jan 13

Diabetic retinopathy in Tanzania: prevalence and risk factors at entry into a regional screening programme
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Objective: The number of adults with diabetes in sub-Saharan Africa (SSA) is expected to almost double by 2035. This study investigated the prevalence of diabetic retinopathy (DR) and its risk factors at entry into a community-based screening programme.
Methods: All persons with diabetes screened for retinopathy at entry into a screening programme in Kilimanjaro Region, Tanzania between November 2010 and December 2014 were included. Fundus photographs were taken with a Topcon retinal camera following pupil dilation. Data were collected on BP, random blood sugar, duration of diabetes, BMI and visual acuity on entry.
Results: A total of 3187 persons were screened for DR. The prevalence of any DR was 27.9% (95%CI 26.4-29.5%) with background diabetic retinopathy (BDR), pre-proliferative diabetic retinopathy (PPDR) and proliferative diabetic retinopathy (PDR) having a prevalence of 19.1% (95% CI 17.7-20.4%), 6.0% (95%CI 5.2-6.8%) and 2.9% (95%CI 2.3-3.5%), respectively. Maculopathy was present in 16.1% (95%CI 14.8-17.4%) of participants. Multivariable logistic regression analysis for the presence of any DR found independent associations with duration of diabetes ($P < 0.0001$), systolic BP ($P < 0.0001$), random blood sugar ($P < 0.0001$) and attending a government hospital diabetic clinic ($P = 0.0339$).
Conclusions: This study is the first to present data from a DR screening programme in SSA. The results will provide policymakers with data to aid planning of DR screening and treatment services in the African region. The study highlights the importance of managing comorbidities within DR screening programmes.

Other

34. TMIH 2016;21(2):158-65. Epub 2015 Dec 14

Prevalence and causes of hearing impairment in Africa
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Objective: To systematically assess the data on the prevalence and causes of hearing impairment in Africa.
Methods: Systematic review on the prevalence and causes of hearing loss in Africa. We undertook a literature search of seven electronic databases (EMBASE, PubMed, Medline, Global Health, Web of Knowledge, Academic Search Complete and Africa Wide Information) and manually searched bibliographies of included articles. The search was restricted to population-based studies on hearing impairment in Africa. Data were extracted using a standard protocol.
Results: We identified 232 articles and included 28 articles in the final analysis. The most common cut-offs used for hearing impairment were 25 and 30 dB HL, but this ranged between 15 and 40 dB HL. For a cut-off of 25 dB, the median was 7.7% for the children- or school-based studies and 17% for population-based studies. For a cut-off of 30 dB HL, the median was 6.6% for the children or school-based studies and 31% for population-based studies. In schools for the deaf, the most common cause of hearing impairment was cryptogenic deafness (50%) followed by infectious causes (43%). In mainstream schools and general population, the most common cause of hearing impairment was middle ear disease (36%), followed by undetermined causes (35%) and cerumen impaction (24%).
Conclusion: There are very few population-based studies available to estimate the prevalence of hearing impairment in Africa. Those studies that are available use different cut-offs, making comparison difficult. However, the evidence suggests that the prevalence of hearing impairment is high and that much of it is avoidable or treatable.

Tuberculosis

35. Lancet 2016;387(10024):1211-26. Epub 2015 Sep 13

Tuberculosis
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Although the worldwide incidence of tuberculosis has been slowly decreasing, the global disease burden remains substantial (~9 million cases and ~1·5 million deaths in 2013), and tuberculosis incidence and drug resistance are rising in some parts of the world such as Africa. The modest gains achieved thus far are threatened by high prevalence of HIV, persisting global poverty, and emergence of highly drug-resistant forms of tuberculosis. Tuberculosis is also a major problem in health-care workers in both low-burden and high-burden settings. Although the ideal preventive agent, an effective vaccine, is still some time away, several new diagnostic technologies have emerged, and two new tuberculosis drugs have been licensed after almost 50 years of no tuberculosis drugs being registered. Efforts towards an effective vaccine have been thwarted by poor understanding of what constitutes protective immunity. Although new interventions and investment in control programmes will enable control, eradication will only be possible through substantial reductions in poverty and overcrowding, political will and stability, and containing co-drivers of tuberculosis, such as HIV, smoking, and diabetes.

36. Lancet 2016 Mar 23. pii: S0140-6736(15)01316-1. [Epub ahead of print]

A blood RNA signature for tuberculosis disease risk: a prospective cohort study
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Background: Identification of blood biomarkers that prospectively predict progression of Mycobacterium tuberculosis infection to tuberculosis disease might lead to interventions that combat the tuberculosis epidemic. We aimed to assess whether global gene expression measured in whole

blood of healthy people allowed identification of prospective signatures of risk of active tuberculosis disease.
Methods: In this prospective cohort study, we followed up healthy, South African adolescents aged 12-18 years from the adolescent cohort study (ACS) who were infected with M tuberculosis for 2 years. We collected blood samples from study participants every 6 months and monitored the adolescents for progression to tuberculosis disease. A prospective signature of risk was derived from whole blood RNA sequencing data by comparing participants who developed active tuberculosis disease (progressors) with those who remained healthy (matched controls). After adaptation to multiplex quantitative real-time PCR (qRT-PCR), the signature was used to predict tuberculosis disease in untouched adolescent samples and in samples from independent cohorts of South African and Gambian adult progressors and controls. Participants of the independent cohorts were household contacts of adults with active pulmonary tuberculosis disease.
Findings: Between July 6, 2005, and April 23, 2007, we enrolled 6363 participants from the ACS study and 4466 from independent South African and Gambian cohorts. 46 progressors and 107 matched controls were identified in the ACS cohort. A 16 gene signature of risk was identified. The signature predicted tuberculosis progression with a sensitivity of 66·1% (95% CI 63·2-68·9) and a specificity of 80·6% (79·2-82·0) in the 12 months preceding tuberculosis diagnosis. The risk signature was validated in an untouched group of adolescents (p=0·018 for RNA sequencing and p=0·0095 for qRT-PCR) and in the independent South African and Gambian cohorts (p values <0·0001 by qRT-PCR) with a sensitivity of 53·7% (42·6-64·3) and a specificity of 82·8% (76·7-86) in the 12 months preceding tuberculosis.
Interpretation: The whole blood tuberculosis risk signature prospectively identified people at risk of developing active tuberculosis, opening the possibility for targeted intervention to prevent the disease.
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